Case Report

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Arias-Stella reaction and frightening cytological changes in endocervical polyp: a rare case report

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ABSTRACT

The Arias-Stella (AS) reaction is hormone-dependent atypical endometrial changes characterized by hyperplasia, hypertrophy, vacuolization, pronounced nuclear atypia, pronounced nuclear pleomorphism, and prominent nuclear hyperchromasia in glandular epithelial cells. It is very rare to see AS-related changes in extra uterine areas, especially in an endocervical polyp. Since this benign lesion is very similar to misdiagnoses such as adenocarcinoma, it is very critical to recognize AS reaction in extrauterine areas. The interpretation of pathological findings involves many difficulties, for example, due to the generally small size and fragmentation. Considering the clinical history and good interpretation of the nuclear details are extremely important for correct diagnosis. Here, we present the frightening cellular changes associated with AS observed in an endocervical polyp encountered after abortion in a middle-aged pregnant woman, together with the literature findings.

Keywords: Endocervical polyp, Arias-Stella reaction, frightening cytological changes

INTRODUCTION

The Arias-Stella (AS) reaction is a benign, proliferative change that usually occurs in the Mullerian epithelium in response to hyperprogestational states (1). In this change, marked hypertrophy and vacuolization in the glands of the epithelium and prominent nuclear pleomorphism, atypia, and hyperchromasia are observed in the nuclei. Although this occurs routinely during pregnancy (normal and external), it can also be observed following gestational trophoblastic diseases and the use of progestational agents (1,2). Although it is most commonly encountered in the glandular epithelium of the endometrium, changes related to the AS reaction have been reported in many extrauterine regions, including the endocervical gland, endocervical polyp, endometriosis, adenomyosis, and tubal epithelium (2,3). Recognition of AS-related changes in the extrauterine regions is very important, as it has the potential to be misinterpreted as serous or clear cell carcinoma or an endometrial intra-epithelial carcinoma (3,4). There are very few publications in the literature describing the AS reaction in endocervical polyp (5,6). Here, we present an endocervical polyp we observed in the abortion material of a middle-aged female patient and the frightening cytological changes due to the AS reaction we observed in this polyp.

CASE

A 41-year-old female patient has an uneventful first-trimester pregnancy. An incidental endocervical polyp was detected during routine prenatal examinations. Her pregnancy was terminated as abortion at the 10th week with abnormal uterine bleeding. In the histopathological examination, an endocervical polyp of 0.5 cm in size was detected between the decidualized fragments and choral elements showing changes related to AS. It was observed that the cells forming the endocervical glands in this polyp randomly had significant nuclear atypia. There were atypical cells, prominent nuclear enlargement, nuclear pleomorphism, nuclear hyperchromasia. Nuclear pseudo inclusions were also observed in these atypical cells. When the chromatin distribution of these cells was examined, it was noted that the chromatin was in the form of staining. Nuclear pseudo inclusions were also observed in these atypical cells (**Figure 1-4**). Glands containing the described changes were surrounded by decidualized stromal cells. There was no increase in mitotic activity in atypical cells, and the basement membrane between epithelial cells and stroma appeared quite smooth and there were no signs of desmoplastic response or invasion. In the applied immunohistochemical study, Napsin

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was positive in atypical cells, while Ki-67 and p53 were not positive. In the presence of current clinical and histopathological findings, the case was interpreted as changes in the endocervical polyp due to AS.

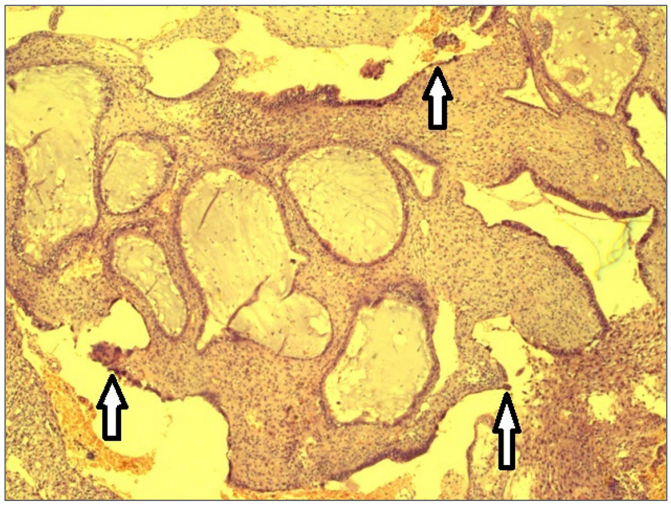

Figure 1. An endocervical polyp has atypical cells interspersed between normal glands in focal areas (arrows) (x4, H&E)

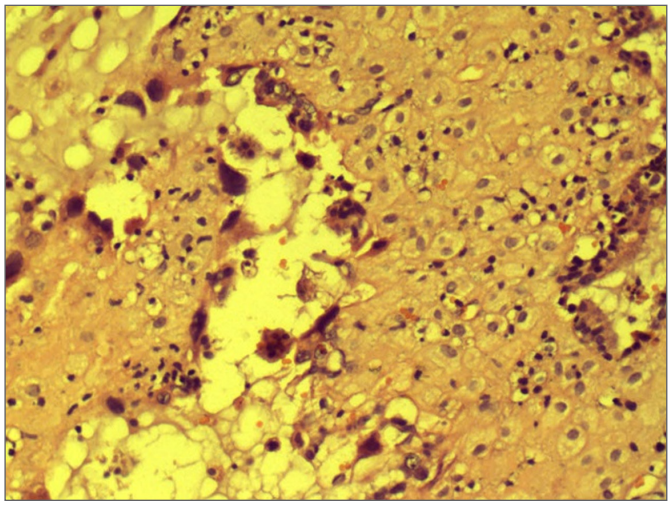

Figure 2. Atypical cells showed striking variability among themselves, and some cells had frightening atypia (x20, H&E).

DISCUSSION

Here, we describe the frightening cytological changes due to AS reaction that we observed in the endocervical polyp in the abortion material of a pregnant patient. AS reaction was first described by Arias-Stella in 1954 in endometrial glands (1). Later, Arias-Stella himself reported that these changes may also occur outside the endometrium (2). AS-related changes in the endocervical glands have been described in many studies in the literature and atypical cells have been described in the smears of these women (3,4). AS-related changes in an endocervical polyp are extremely rare and were first reported by Cariani et al. (5) in 1966. In 1995, McCormick et al. (6) reported tripolar mitosis secondary to AS reaction in an endocervical polyp. In our case, there were terrible cytological changes due to AS reaction in an endocervical polyp. Due to its rarity and cytological changes, our case makes an important contribution to the literature.

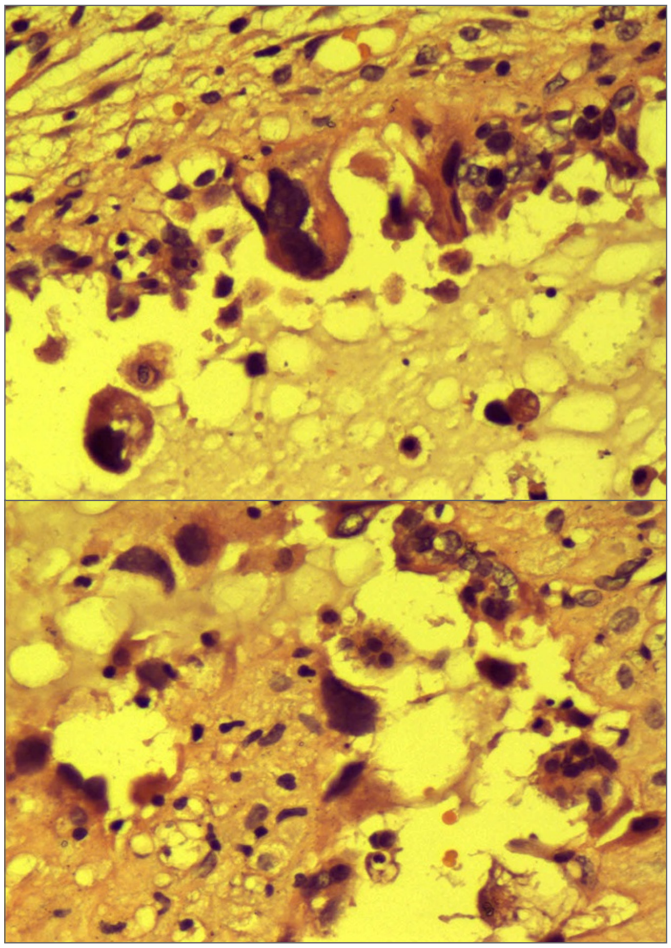

Figure 3,4. Despite this frightening appearance in atypia, there was no increase in mitotic activity and changes in nuclear chromatin were degenerative (x40, H&E).

Five different histological and cytological variants of AS reaction have been reported to date. These are minimal atypia, early secretory pattern, secretory or hypersecretory pattern, proliferative or nonsecretory pattern, and monster cell pattern (1,2). The secretory or hypersecretory pattern, which is the most frequently encountered one and defined as the classical pattern, is characterized by diffuse cytoplasmic vacuolization in the glands and hyperchromasia in the nuclei (2). Monster cell pattern, on the other hand, is the least encountered and the most difficult to diagnose variant, characterized by the presence of highly pleomorphic, large and odd nuclei containing inclusions (7). The AS reaction in endocervical glands often shows a monster cell pattern, further increasing the diagnostic difficulties (7,8). This pattern was also widely observed in our case and the following criteria were used to overcome the diagnostic pitfalls.

The histological diagnosis of AS reaction should be made independently of the organ in which it is seen and is possible by microscopic analysis of routine hematoxylin-

eosin stained sections. The cytological features of the AS reaction seen in the endocervical glands are generally similar to the endometrium, but it is typical that cells that appear strikingly pleomorphic are located between cells with normal morphology (9-13). Napsin, Ki-67 and p53 can be preferred for immunohistochemical study. The benefit of estrogen and progesterone is limited (11). Although the histopathological analysis of our case had some difficulties due to the small size of the polyp, the diagnosis was made safely with the following clinicopathological criteria. First, atypical cells were located focally interspersed between normal glands. Second, there was marked variation among atypical cells, and the atypia in some cells was quite frightening. Third, despite this apparent atypia, the nuclear changes were stained, that is, degenerative/regenerative, and there was no mitotic activity. Fourth, the stroma under the pleomorphic glands was quite smooth without desmoplastic reaction and there was evidence of decidualization in the surrounding stromal cells. Finally, while Napsin positivity was present in atypical cells, Ki-67 and p53 staining were not observed. When the clinical pregnancy history of the case was added to these findings, the morphological changes were interpreted in the context of AS.

Of the lesions of the endocervix to be confused with AS, two entities should be noted: microglandular hyperplasia and clear cell adenocarcinoma (14). Although the AS reaction in the endocervical region is focal, it has been described in 10% of pregnancies. It is often focal and is observed in the superficial glands of the cervical canal (14,15). Histologically, it consists of cells with highly atypical and hyperchromatic nuclei, with eosinophilic and vacuolated cytoplasm, similar to those in the endometrium. Typically, these pleomorphic cells are located between normal-appearing cells and mitosis is rare (15,16). The relationship between microglandular hyperplasia and hormonal status remains unclear. Morphologically, it is characterized by densely packed, irregularly shaped glands with varying degrees of cystic dilation (17). These glands contain mucin and are vacuolated. Although focal atypia is observed, cells are generally similar in size and shape, and mitotic activity is low (17,18). Although clear cell carcinoma is often associated with diethylstilbestrol exposure in utero, it can occur without a history of this exposure (19). It often presents with a mass. Morphologically, it exhibits an infiltrative and irregular growth pattern. It is very useful to evaluate this pattern at small magnification (19, 20). At low magnification, the glands of the AS reaction will show a structure compatible with the regular distribution of normal endocervical glands, while the glands of clear cell carcinoma will show an irregular distribution (20). In addition, cells in clear cell carcinoma exhibit a solid and papillary pattern, and mitotic activity is increased. Rare tumours that can be included in the differential diagnosis include metastatic renal cell carcinoma, mesonephric hyperplasia, and steroid cell tumours. Clinical, morphological and immunohistochemical studies are very useful in distinguishing these tumours (21).

CONCLUSION

Although AS reaction is very common in daily practice, especially in pregnant women, it is very important to keep in mind and diagnose these seemingly simple changes outside of the endometrial glands, as misdiagnosis of lesions included in the differential diagnosis can lead to severe consequences.

ETHICAL DECLARATIONS

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version

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